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     (FILE 'HOME' ENTERED AT 18:50:04 ON 15 JUL 2004)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:50:16 ON 15 JUL
     2004
L1            52 S SURFACE(W)ELECTRICAL(W)CAPACITANCE
L2       1004389 S SKIN
L3            42 S L1 AND L2
L4            16 S PF AND L3
L5             5 DUP REM L4 (11 DUPLICATES REMOVED)
L6            18 DUP REM L3 (24 DUPLICATES REMOVED)
L7         82261 S HUMAN(3A)SKIN
L8            16 S L1 AND L7
L9             7 S L8 AND PF
L10            3 DUP REM L9 (4 DUPLICATES REMOVED)

=> d au ti so ab 1-5 l5

L5   ANSWER 1 OF 5     MEDLINE on STN                    DUPLICATE 1
AU   Boyce S T; Supp A P; Swope V B; Warden G D
TI   Topical sulfamylon reduces engraftment of cultured skin
     substitutes on athymic mice.
SO   Journal of burn care & rehabilitation, (1999 Jan-Feb) 20 (1 Pt 1) 33-6.
     Journal code: 8110188. ISSN: 0273-8481.
AB   Sulfamylon (mafenide acetate) remains extremely valuable for the control
     of the bacterial contamination of burn wounds, but it is cytotoxic to
     cultured keratinocytes used for wound closure.  Because composite
     skin substitutes develop a partial epidermal barrier in vitro,
     they may hypothetically tolerate the use of topical Sulfamylon.  To test
     this hypothesis, cultured skin substitutes were prepared from
     cultured human fibroblasts; keratinocytes were attached to these
     collagen-based substrates, which were grafted to full-thickness wounds in
     athymic mice (n = 8 per group).  Wounds were irrigated twice daily with 5%
     (wt/vol) Sulfamylon solution or with a formulation of noncytotoxic
     antimicrobials (0% Sulfamylon).  On day 9 after grafting, the wounds were
     treated with dry dressings and assessed at 4 weeks for expression of human
     leukocyte antigens-A, B, C and at 2, 3, and 4 weeks for percentage of
     original wound area and surface electrical
     capacitance in picofarads (pF).  Data were analyzed for
     statistical significance (P < .05) by Fisher's exact test, Student's t
     test, and repeated measures analysis of variance: [table: see text] The
     data demonstrate that irrigation of cultured skin substitutes
     with a solution of 5% Sulfamylon results in smaller wound area, fewer
     wounds that contain human cells, and greater surface hydration (higher
     surface electrical capacitance) than
     irrigation with noncytotoxic antimicrobial agents.  These results support
     the conclusion that cultured skin substitutes of this type do
     not tolerate the chemical toxicity of Sulfamylon as well as skin
     autografts.  Further improvements in the properties of the epidermal
     barrier of cultured skin substitutes may facilitate the use of
     Sulfamylon or other potent antimicrobial agents for the management of
     microbial contamination during engraftment of transplanted skin
     cells.

L5   ANSWER 2 OF 5     MEDLINE on STN                    DUPLICATE 2
AU   Boyce S T; Supp A P; Harriger M D; Pickens W L; Wickett R R; Hoath S B
TI   Surface electrical capacitance as a
     noninvasive index of epidermal barrier in cultured skin
     substitutes in athymic mice.
SO   Journal of investigative dermatology, (1996 Jul) 107 (1) 82-7.
     Journal code: 0426720. ISSN: 0022-202X.
AB   Restoration of an epidermal barrier is a definitive requirement for wound
```

closure. To determine formation of an epidermal barrier as a function of hydration of the stratum corneum, we measured **surface electrical capacitance** (SEC) of the epidermis in cultured **skin** substitutes (CSS) in vitro and after grafting to athymic mice. CSS were prepared from human keratinocytes and fibroblasts attached to collagen-glycosaminoglycan substrates. On culture days 3, 7, 14, 17, and 21, SEC was measured in situ. CSS (n = 18; mean +/- SEM) showed a time-dependent decrease of SEC (picoFarads, "**pF**") from 4721 +/- 28 **pF** on day 3 to 394 +/- 117 **pF** on day 14, and subsequent increase to 1677 +/- 325 **pF** on day 21. After 14-d incubation, parallel CSS samples (n = 5) or murine autografts (n = 5) were grafted orthotopically to athymic mice. After grafting, CSS showed decreases in SEC from 910 +/- 315 **pF** at 2 wk to 40 +/- 10 **pF** at 4 wk with no significant decreases thereafter. Control values for murine autograft were 870 +/- 245 **pF** at 2 wk, and 87 +/- 30 **pF** at 4 wk. SEC values for native murine **skin** (n = 10) were 91 +/- 18 **pF**, and for native human **skin** (n = 10) were 32 +/- 5 **pF**. The data demonstrate that SEC decreases with time in culture and that healed or intact **skin** has approximately 10- to 100-fold lower SEC than CSS in vitro. This noninvasive technique provides a quantitative index of epidermal barrier in CSS in vitro and demonstrates the development of functional epidermal barrier during healing of wounds treated with cultured **skin** substitutes.

L5 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 3

AU Okah F A; Wickett R R; Pickens W L; Hoath S B

TI **Surface electrical capacitance** as a noninvasive bedside measure of epidermal barrier maturation in the newborn infant.

SO Pediatrics, (1995 Oct) 96 (4 Pt 1) 688-92.
Journal code: 0376422. ISSN: 0031-4005.

AB OBJECTIVE. The classical studies of epidermal barrier function in infants have relied on measurement of transepidermal water loss by evaporimetry. This technique, although valuable, is, in practice, slow, expensive, and susceptible to error because of convective air currents. In this prospective study, we evaluated gestation-dependent and postnatal age-dependent changes in epidermal barrier function by measurement of **skin surface electrical capacitance** (SEC) in 40 newborn infants ranging from 25 to 40 weeks' gestational age. SEC was measured in picofarads with a dermal phase meter. METHODOLOGY. The measurements were recorded continuously during a 12-second period from the forehead at 12 to 24 hours of life. The baseline (CBL) surface hydration at 1 second and the rate of change of SEC during probe occlusion (CSL) were used as measures of surface hydration and transepidermal water movement, respectively. In the most premature infants (< 30 weeks), these measurements were repeated daily for 5 days. Data were analyzed by analysis of variance after logarithmic (Ln) transformation. RESULTS. We found a significant difference in Ln(CBL) in infants born before and after 30 weeks' gestation (4.91 +/- 0.36 Ln[**pF**] vs 2.67 +/- 0.21 Ln[**pF**], respectively). Similarly, CSL was significantly different in infants born before and after 30 weeks' gestation (16.42 +/- 5.55 **pF**/s vs 1.59 + 0.22 **pF**/s, respectively). In infants born at less than 27 weeks, both Ln(CBL) and CSL decreased significantly by postnatal day 5. In the term group (n = 25), CSL was significantly greater in white than in black infants (1.96 +/- 1.32 **pF**/s vs. 0.95 +/- 0.55 **pF**/s, respectively). CONCLUSION. These results demonstrate impaired epidermal barrier properties in immature infants, less than 30 weeks' gestation, and reveal a remarkable rate of barrier maturation of this group in the first few days of postnatal life. Also, the finding of decreased CSL in black infants supports the hypothesis of differences in barrier function attributable to **skin** types. Overall, these findings demonstrate the feasibility of bedside SEC measurements in the evaluation of epidermal barrier properties in the

newborn infant.

L5 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 4
AU Okah F A; Pickens W L; Hoath S B
TI Effect of prenatal steroids on **skin** surface hydrophobicity in the premature rat.
SO Pediatric research, (1995 Apr) 37 (4 Pt 1) 402-8.
Journal code: 0100714. ISSN: 0031-3998.
AB The **skin** surface of the newborn rat at term is highly hydrophobic. This surface hydrophobicity plays a putative role in the transition from an aqueous to a gaseous environment at birth and is dependent on the presence of an intact periderm. Glucocorticoids given to pregnant dams, during late gestation, will accelerate formation of the stratum corneum and reduce transepidermal water loss in prematurely delivered pups. We tested the related hypotheses that surface hydrophobicity and maturation of the periderm are developmentally accelerated by prenatal exposure to steroids. Thirty pregnant Sprague-Dawley rats received either normal saline or 0.5 mg/kg betamethasone on d 17 of gestation. After cesarean delivery on d 18, 19, and 20, dorsal **skin** surface hydrophobicity was quantified by direct **surface electrical capacitance** (SEC) measurement. Initial **skin** surface hydration at birth was significantly lower in steroid-treated pups than in control pups at gestational ages 19 and 20 d (3060 +/- 1379 versus 4441 +/- 153 **pF** and 646 +/- 295 versus 1493 +/- 1019 **pF**, respectively, $p < 0.001$, mean +/- SD). Likewise, after desorption of amniotic fluid, baseline **skin** hydration was significantly lower in steroid-treated pups than in control pups at gestational ages 19 and 20 d (1862 +/- 1560 **pF** versus 4278 +/- 97 **pF** and 60 +/- 56 **pF** versus 128 +/- 264 **pF**, $p < 0.001$). Scanning and transmission electron microscopy showed morphologic maturation of the periderm after steroid treatment. These results demonstrate accelerated development of both functional and structural correlates of **skin** surface hydrophobicity in the premature rat after prenatal exposure to steroids.

L5 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 5
AU Okah F A; Wickett R R; Pompa K; Hoath S B
TI Human newborn **skin**: the effect of isopropanol on **skin** surface hydrophobicity.
SO Pediatric research, (1994 Apr) 35 (4 Pt 1) 443-6.
Journal code: 0100714. ISSN: 0031-3998.
AB The development of a hydrophobic **skin** surface in newborn mammals such as the rat plays an important role in promoting adaptation to the abrupt change in the environment that occurs at birth. To determine whether the **skin** surface plays a similar role in the human neonate, we performed tests of water sorption and desorption on the chest wall of 13 term newborns. These tests were performed within the first 24 h of life on unperturbed **skin** (controls) and after perturbation of a contralateral site with isopropanol. The degree of surface hydration was determined by measurement of **skin surface electrical capacitance**, and desorption rates were calculated by 1st-order kinetic analysis. The unperturbed surface of the newborn **skin** exhibited a peak sorption value (change from baseline after water loading) of 435 +/- 83 **pF** (mean +/- SEM) and a desorption rate of 0.048 +/- 0.009 s-1. After exposure to isopropanol, the peak sorption value increased to 594 +/- 79 **pF** ($p < 0.05$) and the desorption rate decreased to 0.024 +/- 0.004 s-1 ($p < 0.01$). Paired sorption values were positively correlated ($r2 = 0.8$, $p < 0.001$). These results support the hypothesis that the **skin** surface of the human newborn, by limiting the sorption of water (or amniotic fluid) on the **skin**, may play a role in the adaptation to the change in environment at birth.

=> d au ti so ab 1-3 l10

L10 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1
AU Boyce S T; Supp A P; Harriger M D; Pickens W L; Wickett R R; Hoath S B
TI **Surface electrical capacitance** as a noninvasive index of epidermal barrier in cultured skin substitutes in athymic mice.
SO Journal of investigative dermatology, (1996 Jul) 107 (1) 82-7. Journal code: 0426720. ISSN: 0022-202X.
AB Restoration of an epidermal barrier is a definitive requirement for wound closure. To determine formation of an epidermal barrier as a function of hydration of the stratum corneum, we measured **surface electrical capacitance** (SEC) of the epidermis in cultured skin substitutes (CSS) in vitro and after grafting to athymic mice. CSS were prepared from human keratinocytes and fibroblasts attached to collagen-glycosaminoglycan substrates. On culture days 3, 7, 14, 17, and 21, SEC was measured in situ. CSS (n = 18; mean +/- SEM) showed a time-dependent decrease of SEC (picoFarads, "**pF**") from 4721 +/- 28 **pF** on day 3 to 394 +/- 117 **pF** on day 14, and subsequent increase to 1677 +/- 325 **pF** on day 21. After 14-d incubation, parallel CSS samples (n = 5) or murine autografts (n = 5) were grafted orthotopically to athymic mice. After grafting, CSS showed decreases in SEC from 910 +/- 315 **pF** at 2 wk to 40 +/- 10 **pF** at 4 wk with no significant decreases thereafter. Control values for murine autograft were 870 +/- 245 **pF** at 2 wk, and 87 +/- 30 **pF** at 4 wk. SEC values for native murine skin (n = 10) were 91 +/- 18 **pF**, and for native **human skin** (n = 10) were 32 +/- 5 **pF**. The data demonstrate that SEC decreases with time in culture and that healed or intact skin has approximately 10- to 100-fold lower SEC than CSS in vitro. This noninvasive technique provides a quantitative index of epidermal barrier in CSS in vitro and demonstrates the development of functional epidermal barrier during healing of wounds treated with cultured skin substitutes.

L10 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
AU OKAH F A; WICKETT R R; PICKENS W L; HOATH S B (Reprint)
TI **SURFACE ELECTRICAL CAPACITANCE** AS A NONINVASIVE BEDSIDE MEASURE OF EPIDERMAL BARRIER MATURATION IN THE NEWBORN-INFANT
SO PEDIATRICS, (OCT 1995) Vol. 96, No. 4, Part 1, pp. 688-692. ISSN: 0031-4005.
AB Objective. The classical studies of epidermal barrier function in infants have relied on measurement of transepidermal water loss by evaporimetry. This technique, although valuable, is, in practice, slow, expensive, and susceptible to error because of convective air currents. In this prospective study, we evaluated gestation-dependent and postnatal age-dependent changes in epidermal barrier function by measurement of skin **surface electrical capacitance** (SEC) in 40 newborn infants ranging from 25 to 40 weeks' gestational age. SEC was measured in picofarads with a dermal phase meter.

Methodology. The measurements were recorded continuously during a 12-second period from the forehead at 12 to 24 hours of life. The baseline (C-BL) surface hydration at 1 second and the rate of change of SEC during probe occlusion (C-SL) were used as measures of surface hydration and transepidermal water movement, respectively. In the most premature infants (<30 weeks), these measurements were repeated daily for 5 days. Data were analyzed by analysis of variance after logarithmic (Ln) transformation.

Results. We found a significant difference in Ln(C-BL) in infants born before and after 30 weeks' gestation (4.91 +/- 0.36 Ln[**pF**] vs 2.67 +/- 0.21 Ln[**pF**], respectively). Similarly, C-SL was significantly different in infants born before and after 30 weeks' gestation (16.42 +/- 5.55 **pF**/s vs 1.59 +/- 0.22 **pF**/s, respectively). In infants born at less than 27 weeks, both Ln(C-BL) and

C-SL decreased significantly by postnatal day 5. In the term group (n = 25), C-SL was significantly greater in white than in black infants (1.96 +/- 1.32 **pF**/s vs. 0.95 +/- 0.55 **pF**/s, respectively).

Conclusion. These results demonstrate impaired epidermal barrier properties in immature infants, less than 30 weeks' gestation, and reveal a remarkable rate of barrier maturation of this group in the first few days of postnatal Life. Also, the finding of decreased C-SL in black infants supports the hypothesis of differences in barrier function attributable to skin types. Overall, these findings demonstrate the feasibility of bedside SEC measurements in the evaluation of epidermal barrier properties in the newborn infant.

L10 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
AU Okah F A; Wickett R R; Pompa K; Hoath S B
TI **Human** newborn **skin**: the effect of isopropanol on skin surface hydrophobicity.
SO Pediatric research, (1994 Apr) 35 (4 Pt 1) 443-6.
Journal code: 0100714. ISSN: 0031-3998.
AB The development of a hydrophobic skin surface in newborn mammals such as the rat plays an important role in promoting adaptation to the abrupt change in the environment that occurs at birth. To determine whether the skin surface plays a similar role in the human neonate, we performed tests of water sorption and desorption on the chest wall of 13 term newborns. These tests were performed within the first 24 h of life on unperturbed skin (controls) and after perturbation of a contralateral site with isopropanol. The degree of surface hydration was determined by measurement of skin **surface electrical capacitance**, and desorption rates were calculated by 1st-order kinetic analysis. The unperturbed surface of the newborn skin exhibited a peak sorption value (change from baseline after water loading) of 435 +/- 83 **pF** (mean +/- SEM) and a desorption rate of 0.048 +/- 0.009 s-1. After exposure to isopropanol, the peak sorption value increased to 594 +/- 79 **pF** ($p < 0.05$) and the desorption rate decreased to 0.024 +/- 0.004 s-1 ($p < 0.01$). Paired sorption values were positively correlated ($r2 = 0.8$, $p < 0.001$). These results support the hypothesis that the **skin** surface of the **human** newborn, by limiting the sorption of water (or amniotic fluid) on the skin, may play a role in the adaptation to the change in environment at birth.

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☐ 2. 20020168768. 01 Mar 02. 14 Nov 02. Skin substitutes with improved barrier function. Comer, Allen, et al. 435/371; 424/93.7 C12N005/08 A61K045/00.

☐ 3. 20020164793. 01 Mar 02. 07 Nov 02. Skin substitutes and uses thereof. Conrad, Paul Barth, et al. 435/371; 424/93.7 C12N005/08 A61K045/00.

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